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Atty. Dkt. No. 034258-1401

REMARKS

Claims 32-46 are pending in this application. Claims 32, 35, 38 and 42-44 have been amended to more clearly define the invention. The amendments find support in the application and originally filed claims. For example, support for covalent binding of a mediator molecule can be found at page 4, lines 4-7. Support for the recited implant materials as amended in claim 44 is found throughout the specification and the claims as originally filed, for example at p. 1, lines 13-23. Accordingly, the present amendments raise no issue of new matter.

Entry of the amendments herein are appropriate as the amendments place the case in better condition for allowance or reduce issues upon appeal.

Rejection under 35 U.S.C. § 112 - Indefiniteness

The rejection of claim 32 and claims depending therefrom as being allegedly indefinite is acknowledged. The Examiner asserts that a "(c)" should be inserted in line 9 of claim 32. Although Applicant does not agree with the basis for the rejection, in order to reduce issues upon appeal, claim 32 has now been amended to include a "(c)" as suggested by the Examiner. Withdrawal of this rejection is respectfully requested.

The rejection of claim 42 as allegedly indefinite is acknowledged. The Examiner asserts there is no antecedent basis for "the metal component," "the metallic alloy component" or "the ceramic component." Although Applicant does not agree with this rejection, in order to reduce issues upon appeal, reference to "component" has been deleted from claim 42 as suggested by the Examiner. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Nevertheless, Applicants submit that there is proper antecedent basis for the terms since claim 32, from which claim 42 depends, recites "wherein the implant material comprises at least one component selected from the group consisting of a metal, a metallic alloy, and a ceramic material." One of ordinary skill would understand and readily determine the scope of the rejected terms as used in claim 42 in view of claim 32 and the specification.

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The rejection of claim 44 as allegedly indefinite is acknowledged. The Examiner asserts that the phrases referring to implant materials do not have proper antecedent basis. As described above, claim 44 has been amended to recite metal, metallic alloy and ceramic as implant materials. This amendment provides express antecedent basis to depend from the implant material in claim 35. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

**Rejections under 35 U.S.C. § 103**

**Rejection under 35 U.S.C. § 103(a) over Sukenikk, in view of Vosika taken with Senter or Mueller**

The rejection of claims 32-37 and 41-45 as allegedly being obvious over Sukenikk, et al. (WO 92/00047) in view of Vosika, et al. (WO 90/09798) taken with Senter, et al. (U.S. Pat. No. 5,306,307) or Mueller, et al. (U.S. Pat. No. 5,837,235), is respectfully traversed.

To establish a prima facie case of obviousness, three criteria must be met; (1) there must be some motivation or suggestion, either in the cited publications or in knowledge available to one skilled in the art, to modify or combine the cited publications; (2) there must be a reasonable expectation of success in combining the publications to achieve the claimed invention; and (3) the publications must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142.

Claims 32-37 and 41-45 are generally directed to a method of producing an implant which has an anchor molecule covalently bound to the surface of a metal, metallic alloy or ceramic implant material. The anchor molecule is then covalently bound to a mediator molecule that reduces rejection of the implant and/or promotes growing-in of the implant.

Applicant respectfully disagrees with the Examiner's assertion that independent claims 32, 35 and 38 do not require covalent bonding between the mediator molecule and the functional group of the anchor molecule. The claims clearly state the functional group is for covalent bonding and that the mediator molecule is to bind to the functional group. One of ordinary skill

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in the art would be able to readily determine from the claim language that binding is to be covalent. However, in order to place the case in better condition for allowance or reduce issues upon appeal, the claims have been amended herein to expressly refer to "covalently" immobilizing a mediator molecule on the implant material using the functional group.

Even if the claim is understood to require covalent immobilization between a mediator molecule and an anchor or spacer molecule, the Examiner nevertheless asserts that such linkage would be obvious. However, the Examiner does not point to a single instance in Sukennik, Senter or Mueller that teaches or suggests to make such covalent bonding. Merely listing functional groups that "could" form a covalent bond falls far short of the necessary teaching required to render obvious the use of such linkage between a mediator molecule and anchor or spacer molecule. Sukennik, Senter and Mueller only describe non-covalent bonding despite the fact that covalent methods of bonding molecules were very well known in the art. The failure to consider or even mention covalent immobilization between a mediator molecule and an anchor or spacer molecule in any of Sukennik, Senter and Mueller must be considered to be a purposeful limitation on the scope of these disclosures.

While the Vosika reference cited by the Examiner discusses covalent bonding, the chemistry disclosed is for covalently linking cytokines to organic material supports, e.g., polystyrene and its not suitable for linking to inorganic materials or metals. Particularly, Vosika does not address the difficulties connected with coupling of biomolecules to surfaces such as metal or ceramics, which require, for example, the activation of a metal surface and the use of silane derivatives as anchor molecules. Merely knowing about covalent bonding is not enough for one of ordinary skill to produce an implant with the combination of implant materials and biomolecules as required by the instant claims. Thus, the Examiner's reliance on Vosika, which teaches a particular covalent linkage chemistry that is not compatible with the materials used by the other cited references, defeats the asserted combination of teachings and any prima facie obviousness rejection.

Applicant respectfully requests reconsideration and withdrawal of the rejection.

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**Rejection under 35 U.S.C. § 103(a) over Sukenikk, in view of Vosika taken with Senter or Mueller and further in view of Matsumoto**

The rejection of claims 38 and 39 as allegedly being obvious over Sukenikk (WO 92/00047) in view of Vosika (WO 90/09798) taken with Senter (U.S. Pat. No. 5,306,307) or Mueller (U.S. Pat. No. 5,837,235) and further in view of Matsumoto (U.S. Pat. No. 4,371,612) is respectfully traversed.

As discussed in detail above, the combination of Sukenikk and Vosika taken in view of Senter or Mueller fails to provide a *prima facie* case of obviousness. The combination of art does not teach or suggest how a mediator molecule may be covalently coupled to an activated implant surface via a spacer molecule which is in turn coupled to an anchor molecule which is in turn coupled to the activated surface of the instant invention.

Matsumoto does not address the deficiencies of the other references because it does not teach or address how to deal with the difficulties connected to coupling biomolecules to surfaces such as metal or ceramics. Instead Matsumoto describes immobilization of biological material, such as enzymes, on microporous, water insoluble acrylonitrile polymers via covalent bonding, with the amino groups of the support material being either directly or via spacer molecules linked to the biological material (column 5, lines 39-65).

Matsumoto does not suggest to use its modified polymers as an implant much less suggest the particular implant materials of the present invention, nor the use of morphogens, such as BMP, to coat the implant surface. Of the twenty examples in the patent application, none even suggest use within a living body. Even if one assumes that Matsumoto's chemistry is applicable to the implant materials of the present invention, there still would be no motivation to one of skill in the art to combine the references as alleged by the Examiner. This is because Matsumoto's chemistry is used for making solid phase supports for industrial processing to obtain the product of enzymatic reactions *in vitro*. See, e.g. Matsumoto, Fig. 1 and column 23. One skilled in the art would not consider industrial enzyme processing to even be relevant to the preparation of

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living body implant materials. Thus, because the cited references alone or in combination fail to provide a prima facie case of obviousness, Applicant respectfully requests reconsideration and withdrawal of the rejection.

**Rejection under 35 U.S.C. § 103(a) over Sukenikk in view of Vosika taken with Senter or Mueller and further in view of Goldstein, and if necessary in further view of Goldstein**

The rejection of claims 46 as allegedly being obvious over Sukenikk (WO 92/00047) in view of Vosika (WO 90/09798) taken with Senter (U.S. Pat. No. 5,306,307) or Mueller (U.S. Pat. No. 5,837,235) and further in view of Goldstein (U.S. Pat. No. 4,002,602), and if necessary in further view of Goldstein (U.S. Pat. No. 4,190,647), is respectfully traversed.

As discussed in detail above, the combination of Sukenikk and Vosika taken in view of Senter or Mueller fails to provide a prima facie case of obviousness. The combination of art does not teach or suggest how a mediator molecule may be covalently coupled to an activated implant surface via a spacer molecule which is in turn coupled to an anchor molecule which is in turn coupled to the activated surface.

Both Goldstein references fail to address the deficiencies of Sukenikk, Vosika, Senter and Mueller because neither teaches covalent bonding of biomolecules onto the implant materials required by the instant claims. The Goldstein references merely describe ubiquitous polypeptide (ubiquitin) but in no way suggest its use with implant materials such as metals or ceramics nor do they address what chemistry would be involved to do so or the difficulties connected to coupling biomolecules to surfaces such as metal or ceramics. Thus, because the cited references alone or in combination fail to provide a prima facie case of obviousness, Applicant respectfully requests reconsideration and withdrawal of the rejection.

**Double Patenting**

The rejections of claims 32-37 and 41-44 under the judicially created doctrine of obviousness-type double patenting over claims 1-6 of United States Patent No. 6,635,269; and claims 38 and 39 in view of Matsumoto et al., is acknowledged. These issues will be addressed

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in due course pending resolution of all other issues in the case, e.g., by submission of a terminal disclaimer or other action as may be appropriate.

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CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims is respectfully requested. At the minimum, Applicants request entry of the amendments herein because they place the case in better condition for allowance or reduce issues upon appeal. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to contact the undersigned so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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